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EXAMINER	
MYERS, CARLA J	
ART UNIT	PAPER NUMBER
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/705,531	LU ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-69* is/are pending in the application.

4a) Of the above claim(s) *2,7-46,48,49 and 52-69* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,47,50 and 51* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the amendment filed December 7, 2006. Applicant's arguments have been fully considered but are not persuasive to overcome all grounds of rejection. All rejections not reiterated herein are hereby withdrawn. This action is made final.

Election/Restrictions

2. This application contains claims 2, 7-46, 48, 49, and 52-69 drawn to an invention nonelected with traverse in the reply of May 22, 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1-69 are pending.

Claims 1, 3-6, 47, 50 and 51 have been examined herein.

Objections

3. In claim 1, the comma following "SEQ ID No. 2" should be replaced with a period.

Maintained Rejections

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 50 and 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 50 and 51 are indefinite over the recitation of "complementary." The specification (page 22) defines complementary nucleic acids as sequences that "hybridize specifically to another polynucleotide sequence." However, this definition is vague since the definition does not set forth what the polynucleotide sequence hybridizes to. Further, the phrase "specific hybridization" is vaguely defined in the specification as referring to the formation of hybrids between a probe and a specific target. It is stated that specific hybridization occurs when, for example, a probe "preferentially hybridizes to a specific target so that a single band is observed on Southern blot." This disclosure is not considered to provide a complete and fixed definition for the phrase "specific hybridization" since the disclosure provides only an example of what might be encompassed by this phrase. Also, the definition does not clearly set forth what constitutes preferential hybridization. The skilled artisan cannot determine the meets and bounds of the claimed invention because the claims do not set forth the conditions for determining whether the polynucleotide has or has not hybridized. It is unclear as to whether such nucleic acids hybridize only to SEQ ID NO: 1 (and thereby are fully complementary to SEQ ID NO: 1) or if such nucleic acids also hybridize with variants of SEQ ID NO: 1 (e.g., variants having 99%, 98%, 95%, 90%, 70% etc identity with SEQ ID NO: 1). In the later case, there are no specific teachings provided in the specification to indicate the cut-off point at which the nucleic acid no longer specifically hybridizes to SEQ ID NO: 1. If the claimed nucleic acid is capable of hybridizing with a nucleic acid that differs from SEQ ID NO: 1 by even 1 nucleotide, then such nucleic acids are not truly specific for SEQ ID NO: 1. Additionally, claims 50 and 51 are indefinite over the recitation of "corresponding." This term is defined in the specification at page 22 as referring to nucleic acid sequences that are "complementary to all or a fragment comprising 10 or more consecutive nucleotides of a reference

polynucleotide or encoding an amino acid sequence at least 70%...identical to an amino acid sequence in a peptide or protein." Since "corresponding" sequences are defined in terms of being complementary, and the term "complementary" is indefinite for the reasons stated above, the phrase "corresponding mRNA sequences" is also indefinite. Corresponding is not an art recognized term to describe the relationship between two nucleic acid sequences. It is not clear as to whether a corresponding mRNA refers to a mRNA encoded by the cDNA of SEQ ID NO: 1 or if this refers to sequences similar to SEQ ID NO: 1 or sequences which map to the same region as SEQ ID NO: 1 or homologues of SEQ ID NO: 1, etc. Because the term "corresponding" has not been clearly defined in the specification and because there is no art recognized definition for this term as it relates to nucleic acid sequences, one of skill in the art cannot determine the meets and bounds of the claimed subject matter.

Response to Arguments:

In the response, Applicants traversed this rejection by stating that although the definition for "complementary" requires that a complementary sequence "specifically hybridizes" to a target sequence, there is no requirement to state what sequence it specifically hybridizes to. This argument has been fully considered but is not persuasive. The rejection is maintained because the specification does not provide a complete and fixed definition for the phrase "complementary" since the specification provides only an example of what may be encompassed by this phrase. Further, in order to determine the meets and bounds of the claimed invention, the skilled artisan must understand what is intended to be encompassed by the phrase "specific hybridization" since this phrase is being relied upon to define what may be encompassed by the term "complementary." Yet, it remains unclear as to whether a nucleic acid that specifically hybridizes to another nucleic acid hybridizes to only that

nucleic acid – i.e., is 100% complementary to the full length nucleic acid of SEQ ID NO: 1 or 2 – or whether such a nucleic acid can hybridize to other nucleic acids sharing some level of complementarity with SEQ ID O: 1 and 2. In the later case, the nucleic acid would not in fact specifically hybridize with SEQ ID NO: 1 or 2 if it also cross-hybridizes with other nucleic acids. Based on Applicants arguments on pages 20-21 of the response, one might interpret the phrase as meaning that the nucleic acids share 100% complementarity over the full length of the nucleic acid molecule. But, given the statements on pages 13-14 of the response, it appears that Applicants would also intend for this term to cover nucleic acids which share any percent complementarity with another nucleic acid in order to allow for some degree of specific or nonspecific hybridization under any hybridization conditions to the undefined nucleic acid. Accordingly, Applicants have argued two different definitions for this phrase and thereby it remains unclear as to which definition is intended to be applied to the claimed invention.

Applicants assert that the term "complementary" is well understood in the art. However, there is no fixed definition for this term in the art. Given the ambiguous definition provided for this term in the specification and Applicants apparent conflicting arguments regarding their interpretation of the meaning of this phrase, it is maintained that one of skill in the art would not be able to determine the meets and bounds of the claimed subject matter.

Applicants further argue that the term "corresponding" is definite. It is asserted that the specification (page 22) states that "a corresponding mRNA sequence of SEQ ID NO: 1 refers to a mRNA molecule transcribed from a polynucleotide comprising SEQ ID NO: 1." However, in fact the specification states "**For example**, a "corresponding mRNA..." (emphasis added). Thereby, the specification does not define the term

"corresponding" as one which refers only to the mRNA transcribed from a polynucleotide of SEQ ID NO: 1. Providing an example of what may be encompassed by a term is not equivalent to providing a clear and complete definition for that term.

5. Claims 1, 3-6, 47, 50 and 51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 1 and 3-6 are drawn to polynucleotides "comprising a sequence of SEQ ID NO: 1 or 2." SEQ ID NO: represents a portion of the cDNA encoding the terminal 74 amino acids of the PINX1 protein (SEQ ID NO: 3). In view of the "comprising" language, the claims encompass nucleic acids of any identity or length flanking the sequence of SEQ ID NO: 2. The 5' nucleotides flanking SEQ ID NO: 2 and the overall functional activity of the claimed polynucleotide. Claims 50 and 51 are drawn to antisense polynucleotides complementary to the mRNA sequence corresponding to the sequence comprising SEQ ID NO: 1. As discussed in paragraph 4 above, the terms "complementary" and "corresponding" have not been clearly defined in the specification. As such, these terms have been given their broadest reasonable interpretation and have been interpreted as including polynucleotides which share any level of sequence complementarity (10%, 20%...70%...80% etc) to SEQ ID NO: 1 or a sequence that shares any level of sequence identity with SEQ ID NO: 1 or a fragment thereof. Accordingly, the claims encompass a very large genus of splice variants, allelic variants,

non-naturally occurring variants and homologues of SEQ ID NO: 1. Additionally, the claims include polynucleotides having any functional activity since the claims do not recite any particular biological activity for the nucleic acid or the encoded polypeptide.

While nucleic acids comprising SEQ ID NO: 1 and nucleic acids consisting of SEQ ID NO: 2 meet the written description requirements, the specification does not provide an adequate written description of the claimed genus of nucleic acids comprising a portion of SEQ ID NO: 1 or 2 or comprising a sequence sharing any level of sequence complementary with SEQ ID NO: 1 or 2 or a portion thereof.

The specification teaches the full length cDNA sequence of SEQ ID NO: 1, which encodes for PINX1. The specification teaches that PINX1 binds to Pin2/TFR1 (page 65) and binds to and inhibits telomerase (page 70). The specification also teaches a fragment of SEQ ID NO: 1 (i.e., SEQ ID NO: 2) which encodes for a peptide which binds to and inhibits telomerase (referred to therein as "TID" – telomerase inhibitory domain). Additionally, a polynucleotide referred to as "PinX1-L1" and comprising SEQ ID NO: 5 is also disclosed. However, the specification does not disclose the functional activity of this polynucleotide or its specific relationship to PinX1.

The specification does not specifically disclose any specific naturally or non-naturally occurring mutants, allelic variants, splice variants or homologues of SEQ ID NO: 1.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the

'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, 1 member of the genus of PINX1 polynucleotides has been identified. No additional nucleotide variations have been disclosed. It is then determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g. restriction map, biological activity of an encoded protein product, etc.). In the instant case, no such identifying characteristics have been provided for any of allelic variants, splice variants, or mutant PinX1 polynucleotides. However, the claims as written are inclusive of a potentially large genus of mutations in the PinX1 gene. While one could contemplate a

nucleotide substitution, deletion or addition at each and every position in the PinX1 gene, such nucleotide variations are not considered to be equivalent to specific nucleotide variations associated with telomerase inhibition. Rather, mutations in the PinX1 associated with telomerase inhibition represent a distinct group of nucleotide variations which are expected to occur at only specific locations within the gene and consist of specific nucleotide alterations. Accordingly, knowledge of the sequence of the wild-type gene does not allow the skilled artisan to envision all of the contemplated polymorphisms encompassed by the claimed genus. Conception of the claimed invention cannot be achieved until reduction to practice has occurred, regardless of the complexity or simplicity of potential methods for isolating additional nucleotide variations. As stated in *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. LTD*, 25 USPQ2d 1016, one cannot describe what one has not conceived.

The general knowledge in the art concerning homologues, mutants, allelic and splice variants does not provide any indication of how modification of the sequence of SEQ ID NO: 1 will effect the functional properties of SEQ ID NO: 1. The structure and function of one molecule does not provide guidance as to the structure and function of other molecules. Therefore, the description of one molecule (SEQ ID NO: 1) is not representative of a genus of homologues, splice, mutant and allelic variants of SEQ ID NO: 1 having unspecified functional activities different from that of SEQ ID NO: 1. A general statement in the specification of a desire to obtain gene sequences, homologues from other species, mutated species, SNPs, polymorphic sequences,

promoter sequences and exogenous sequences is not equivalent to providing a clear and complete description of specific sequences which fall within the claimed genus of nucleic acids.

Accordingly, the disclosure in the specification of 1 PinX1 polynucleotide is not considered to constitute a representative number of the splice variants, allelic variants, mutants and homologues of PinX1 encompassed by the claims. For these reasons, Applicants have not provided sufficient evidence that they were in possession, at the time of filing, of the invention as it is broadly claimed and thus the written description requirement has not been satisfied for the claims as they are broadly written. Applicants attention is drawn to the Guidelines for the Examination of Patent Applications under 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Response to arguments:

In the response, Applicants state that it is unclear as to why a nucleic acid comprising SEQ ID NO :1 would be deemed to meet the written description requirements, while a nucleic acid comprising SEQ ID NO: 2 does not meet the written description requirements. As discussed in detail in the above rejection, SEQ ID NO: 1 consists of the full length nucleic acid encoding the full length PINX1 protein which binds to and inhibits telomerase. SEQ ID NO: 2, on the other hand, consists of only a fragment of SEQ ID NO: 1 and encodes for only the terminal 74 amino acids of the PINX1 protein (SEQ ID NO: 3). In view of the "comprising" language, the claims encompass nucleic acids that contain SEQ ID NO: 2 and which further contain an

unspecified number of nucleotides of any identity flanking the 5' sequences of SEQ ID NO: 2. The claims also do not define the functional activity of a nucleic acid comprising SEQ ID NO: 2. Thereby, the claims read on allelic variants and splice variants of a full length PINX nucleic acid in which only 222 nucleotides have been defined in terms of their structure, but in which the overall structure of the nucleic acid (i.e., the 5' nucleotides) and the functional activity of the nucleic acid are not defined. Given that the specification teaches only one PINX1 nucleic acid (SEQ ID NO: 1), this disclosure is not sufficient to establish that Applicants were in possession of the more broadly claimed genus encompassed by the claims of allelic / mutant variants and splice variants of SEQ ID NO: 1.

Regarding claims 50 and 51, Applicants traverse this rejection by stating that the claims do not include antisense oligonucleotides of "any level of sequence complementarity" but rather require that the oligonucleotides be complementary as defined in the specification (i.e., at least able to produce a single band corresponding to said hybridization identifiable on a Southern or Northern blot of DNA or RNA." This argument has also been fully considered but is not persuasive. Applicants arguments mischaracterize the teachings of the specification because the specification does not in fact provide this definition for the term "complementary." Rather, the specification (page 22) states that this is one example of what might be encompassed by the term "complementary." Even if the claims were amended to recite this definition for the term, such a limitation would not provide a meaningful description of the degree of complementarity shared between the claimed oligonucleotides and SEQ ID NO: 1. The

response and specification as originally filed do not clarify what degree of complementarity would be required for the nucleic acid to hybridize to produce a single band on a Southern or Northern blot. That is, what percent complementarity is required to produce a single hybridization band? What length of nucleic acid would produce a single hybridization band? No evidence has been provided to establish that nucleic acids sharing, for example, 70% complementarity with SEQ ID NO: 1 and including only a portion of SEQ ID NO: 1 would not also hybridize with SEQ ID NO: 1 and produce a single band on the gel. Accordingly, it is maintained that the claims read on nucleic acids sharing, for example, 70% identity with fragments of SEQ ID NO: 1, and thereby the claims encompass allelic/ mutant variants and splice variants of SEQ ID NO: 1. Again, the disclosure in the specification of a single nucleic acid comprising SEQ ID NO: 1 does not constitute a representative number of the nucleic acids encompassed by the claims. Applicants have not provided sufficient evidence that they were in possession, at the time of filing, of the invention as it is broadly claimed. Therefore, the rejection is maintained.

6. Claims 1, 3-6, 47, 50 and 51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated polynucleotides comprising SEQ ID NO: 1 and isolated polynucleotides consisting of SEQ ID NO: 2, does not reasonably provide enablement for polynucleotides comprising SEQ ID NO: 2 or comprising a sequence complementary to or corresponding to SEQ ID NO: 1 or 2. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in formulating this rejection (*In re Wands,* 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

Breadth of the Claims:

Claims 1, 3-6 and 47 encompass polynucleotides comprising SEQ ID NO: 2. SEQ ID NO: 2 represents a portion of the cDNA encoding the terminal 74 amino acids of the PINX1 protein (SEQ ID NO: 3). Claims 1, 3-6 and 47 do not define the 5' nucleotides flanking SEQ ID NO: 2 or the overall functional activity of the claimed polynucleotide. Claims 50 and 51 are drawn to antisense polynucleotides complementary to the mRNA sequence corresponding to the sequence comprising SEQ ID NO: 1. As discussed in paragraph 4 above, the terms "complementary" and "corresponding" have not been clearly defined in the specification. As such, these terms have been given their broadest reasonable interpretation and have been interpreted as including polynucleotides which share any level of sequence complementarity (10%, 20%...70%...80% etc) to SEQ ID NO: 1 or a sequence that shares any level of sequence identity with SEQ ID NO: 1 or a fragment thereof. Accordingly, the claims encompass a potentially very large genus of splice variants, allelic variants, non-

naturally occurring variants and homologues of SEQ ID NO: 1. Additionally, the claims include polynucleotides having any functional activity since the claims do not recite any particular biological activity for the nucleic acid or the encoded polypeptide.

Nature of the Invention:

The claims are drawn to polynucleotides comprising SEQ ID NO: 1 or 2 or fragments thereof. The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F. 3d 1316, 1330 (Fed Cir. 2001).

State of the Art:

The specification teaches the full length cDNA sequence of SEQ ID NO: 1, which encodes for PINX1. The specification teaches that PINX1 binds to Pin2/TFR1 (page 65) and binds to and inhibits telomerase (page 70). The specification also teaches a fragment of SEQ ID NO: 1 (i.e., SEQ ID NO: 2) which encodes for a peptide which binds to and inhibits telomerase (referred to therein as "TID" – telomerase inhibitory domain). Additionally, a polynucleotide referred to as "PinX1-L1" and comprising SEQ ID NO: 5 is also disclosed. The PinX1-L1 amino acid sequence shares 73% identity with the amino acid sequence encoded by SEQ ID NO :1 (see Figure 12). However, the specification does not disclose the functional activity of this polynucleotide or its specific relationship to PinX1.

The Predictability or Unpredictability of the Art and Degree of Experimentation:

The prior art acknowledges the unpredictability in modifying the nucleotide sequence of a gene. Modification of even a single nucleotide within a coding or non-

coding sequence can significantly alter the functional properties of that gene and protein encoded thereby. While the specification teaches that the C-terminal domain of the PinX1 polypeptide is important for telomerase binding activity, the specification does not teach any particular amino acids therein which are critical for maintaining binding activity and does not teach any particular nucleotides within the full length PinX1 polynucleotide which encode for amino acids that are critical for other functional activities and/or for maintaining the three dimensional structure of the encoded protein. Thereby, it is highly unpredictable as to how modifying sequences within SEQ ID NO: 1 will effect the overall functional properties of the resulting gene and polypeptide encoded thereby. It is also unpredictable as to how adding nucleotides of any identity or length to the terminus of SEQ ID NO: 2 or to fragments of 1, 2, 3 etc nucleotides of SEQ ID NO: 1 or 2 will effect the functional properties of the resulting nucleic acid and encoded polypeptide.

Amount of Direction or Guidance Provided by the Specification:

The specification does not provide any specific guidance as to how to predictably make and use nucleic acids comprising any portion of SEQ ID NO: 1 or 2 flanked by nucleotides of any length and identity. While one could generate a significantly large genus of nucleic acids in which nucleotides of any identity are added to the 5' or 3' terminus of SEQ ID NO: 2 or fragments of SEQ ID NO: 1 or 2 or in which any number of nucleotides within SEQ ID NO: 1 or 2 are mutated via substitution, addition or deletion, and then assay each of these nucleic acids to try to determine their biological activity, such trial-by-error experimentation is considered to be undue. Providing methods for

searching for additional nucleic acids and trying to determine the function of the resulting nucleic acid or trying to establish an association between the nucleic acids and asthma is not equivalent to teaching how to make and use specific nucleic acids.

Working Examples:

Again, the specification teaches only a full length cDNA comprising SEQ ID NO: 1 and one fragment thereof – i.e. a polynucleotide consisting of SEQ ID NO: 2, wherein said polynucleotide encodes for a polypeptide which binds Pin2/TRF-1 and telomerase . The specification does not provide any working examples of how to predictably make and use nucleic acids comprising SEQ ID NO: 2 or comprising fragments of SEQ ID NO: 1 or 2. There is no disclosure in the specification of additional nucleic acids which contain any number or identity of nucleotides flanking the recited polymorphisms, other than nucleic acids which contain the sequences of SEQ ID NO: 1 or which consist of the sequence of SEQ ID NO: 2. In particular, there are no specific working examples provided in the specification of splice variants, mutants or allelic variants of PinX1 which have a specific and useful functional activity.

Conclusions:

Case law has established that "(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. *In re Fisher,* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that "(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of

guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art. Furthermore, the Court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that "(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement". In the instant case, the claims do not bear a reasonable correlation to the scope of enablement because the specification teaches only 1 members of the broadly claimed genus of nucleic acids, namely SEQ ID NO: 1, whereas the claims encompass a significantly large genus of nucleic acids, in which the overall structural and functional properties of the nucleic acids are not defined. As set forth above, in view of the unpredictability in the art, extensive experimentation would be required to make and use the broadly claimed genus of homologues, mutant, allelic and splice variants of SEQ ID NO: 1 because the specification does not provide sufficient guidance as to how to select the nucleotides which may flank fragments of SEQ ID NO: 1 or 2 or how to select nucleotides within SEQ ID NO: 1 or 2 that may be modified by insertion, deletion or substitution and does not teach a predictable means for determining the functional properties of such nucleic acids. Accordingly, although the level of skill in the art of molecular biology is high, given the lack of disclosure in the specification and in the prior art, it would require undue experimentation for one of skill in the art to make and use the broadly claimed invention.

Response to Arguments:

In the response, Applicants state that the claims have been amended to recite "comprising the sequence of SEQ ID NO: 1 or SEQ ID NO: 2." However, this

amendment does not overcome the rejection as it pertains to the fact that the claims encompass nucleic acid comprising SEQ ID NO: 2 (i.e., a fragment of 222 nucleotides encoding only the terminal 74 amino acids of SEQ ID NO: 3). Again, the claims do not define the nucleotides flanking the 5' sequence of SEQ ID NO: 2 in terms of their identity or length and do not define the overall functional properties of the claimed nucleic acids. Further, claims 50 and 51 read on nucleic acids sharing an undefined level of sequence complementarity with any mRNA that might "correspond" in some manner to SEQ ID NO: 1. Accordingly, the claims encompass a potentially very large genus of splice variants, allelic variants, non-naturally occurring variants and homologues of SEQ ID NO: 1, which are not described in terms of any particular biological activity for the nucleic acid or the encoded polypeptide. Given the lack of specific guidance provided in the specification as to how to modify the sequence of SEQ ID NO: 1 without altering its biological activity, the unpredictability in the art of making and using variants of nucleic acids, and the lack of a teaching in the specification of a representative number of species within the broadly claimed genus, it is maintained that it would require undue experimentation for one of skill in the art to make and use the broadly claimed invention.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 50 and 51 are rejected under 35 U.S.C. 102(a) as being anticipated by Liao et al (Hepatology. Oct 2000. 32: 721-727; cited in the IDS).

Liao et al (Figure 1; deposited as GenBank Accession NO: AF205718 – see page 721) teach a LPTS polynucleotide that encodes the first 132 amino acid residues encoded by SEQ ID NO: 1. The nucleic acid of Liao shares 59% identity and 93% best local similarity with nucleotides 19-1302 of SEQ ID NO: 1 (see below). Accordingly, Liao teaches a polynucleotide comprising a portion of SEQ ID NO: 1 and 2 and thereby anticipates the claimed invention. With respect to claims 3 and 4, Liao et al (page 722) further teaches vectors and host cells comprising said polynucleotide. With respect to claims 5 and 6, Liao et al (page 722) teaches a radioactively labeled 800 nucleotide fragment of the LPTS polynucleotide. With reference to claims 50 and 51, the polynucleotide solutions taught by Liao et al are considered to be pharmaceutical compositions because these solutions could be used for pharmaceutical purposes.

Response to Arguments:

In the response, Applicants state that Laio does not teach a polynucleotide comprising the sequence of SEQ ID NO: 1 or 2. This argument is not persuasive because it is not directed to limitations recited in the claims since claims 50 and 51 are not limited to a polynucleotide comprising the sequence of SEQ ID NO: 1 or 2.

7. Claims 50 and 51 are rejected under 35 U.S.C. 102(a) as being anticipated by Liao et al (GenBank Accession No. AF205718).

The claims are drawn to an isolated PinX1 polynucleotide comprising a sequence

of SEQ ID NO: 1 or 2. In view of the recitation in the claims of "a sequence," the claims have been interpreted as including a polynucleotide comprising a portion of SEQ ID NO: 1 or 2.

Liao teaches a polynucleotide that encodes the first 132 amino acid residues encoded by SEQ ID NO: 1. The nucleic acid of Liao shares 59% identity and 93% best local similarity with nucleotides 19-1302 of SEQ ID NO: 1 (see alignment in paragraph 5 above). Accordingly, Liao teaches a polynucleotide comprising a portion of SEQ ID NO: 1 and 2 and thereby anticipates the claimed invention. With respect to claims 3 and 4, Liao et al further teaches vectors and host cells comprising said polynucleotide. With reference to claims 50 and 51, the polynucleotide solutions taught by Liao et al are considered to be pharmaceutical compositions because these solutions could be used for pharmaceutical purposes.

Response to Arguments:

In the response, Applicants state that Laio does not teach a polynucleotide comprising the sequence of SEQ ID NO: 1 or 2. This argument is not persuasive because it is not directed to limitations recited in the claims since claims 50 and 51 are not limited to a polynucleotide comprising the sequence of SEQ ID NO: 1 or 2.

8. Claims 50 and 51 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillman et al (WO 99/57270).

The claims are drawn to an isolated PinX1 polynucleotide comprising a sequence of SEQ ID NO: 1 or 2. In view of the recitation in the claims of "a sequence," the claims have been interpreted as including a polynucleotide comprising a portion of SEQ ID NO:

1 or 2.

Hillman et al teaches a polynucleotide that shares 99% identity with nucleotides 19 to 1302 of SEQ ID NO: 1. Hillman also teaches a polynucleotide that comprises fragments which are 100% identical to fragments of SEQ ID NO: 1 and 2 (e.g., nucleotides 136-464 of Hillman are 100% identical to nucleotides 19-346 of SEQ ID NO: 1; see alignment below). Accordingly, Hillman teaches a polynucleotide comprising a portion of SEQ ID NO: 1 or SEQ ID NO: 2 and thereby anticipates the claimed invention. With respect to claims 3 and 4, Hillman et al (page 7) further teaches vectors and host cells comprising said polynucleotide. With respect to claims 5 and 6, Hillman (page 27) teaches a labeling the polynucleotide with a detectable moiety, such as a radiolabel, fluorescent label, chemiluminescent label or chromogenic agent. With reference to claims 50 and 51, Hillman (pages 29 and 36-37) teaches polynucleotide solutions to be used for pharmaceutical purposes. which solutions are considered to include a pharmaceutically-acceptable carrier since the solutions are used for pharmaceutical purposes.

Response to Arguments:

In the response, Applicants state that Hillman teaches a nucleic acid that has 99% identity with a portion of SEQ ID NO: 1 and 2, but does not teach a polynucleotide comprising the sequence of SEQ ID NO: 1 or 2. This argument is not persuasive because it is not directed to limitations recited in the claims since claims 50 and 51 are not limited to a polynucleotide comprising the sequence of SEQ ID NO: 1 or 2.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is 571-272-0747. The examiner can normally be reached on Monday-Thursday (6:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Carla Myers

Art Unit 1634

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CARLA J. MYERS
PRIMARY EXAMINER